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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/549,323	09/26/2005	Frank Striggow	LNK-007	8223

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EXAMINER	
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ART UNIT	PAPER NUMBER
1655	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/549,323	STRIGGOW ET AL.	
	Examiner	Art Unit	
	Amy L. Clark	1655	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *15 April 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-19* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-19* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

Claims 3-14, 18 and 19, which were previously withdrawn from consideration as a result of a restriction requirement, are hereby rejoined. Please note that rejoinder is based upon the fact that many of the claimed compounds, with the exception of the ones rejected under 112 1st paragraph, are inherently or intrinsically found in certain types of *Boswellia* species and because it was known in the art that Alzheimer's disease was treatable with boswellic acid and certain extracts and compounds (provided below) obtained from certain *Boswellia* species.

Because all claims previously withdrawn from consideration under 37 CFR 1.142 have been rejoined, **the restriction requirement as set forth in the Office action mailed on 07/27/2007 is hereby withdrawn**.

Please note that Applicants' election of cerebral ischemia and apoplexy still stands, but that the Application is being examined based upon what Applicants are enabled for, so the art may reflect a different enabled use, which is set forth below. Please note that this does not lift the specie election requirement with regards to the disease elected by Applicants.

Claims 1-19 are currently pending and are under examination.

Claim Objections

Claim 1 is objected to because of the following informalities: Please correct lines 8-11 to read: "a hydrogenation product of *Boswellia serrata*, wherein the hydrogenation

product of *Boswellia serrata* is obtained through ~~the~~ catalytic hydrogenation of ethanol extracts of ~~frankincense (~~*Boswellia serrata*~~)~~". Appropriate correction is required.

Response to Arguments

Claim Rejections - 35 USC § 112

Claims 1-19 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of treating Alzheimer's disease comprising administering to a patient in need of such a treatment, an effective dosage of the medicament comprising at least one of the following: incense (olibanum), incense extract, biologically active substances contained in incense and boswellic acid, wherein the extracts are obtained by extraction with (4.2-5.9:1) chloroform: methanol, does not reasonably provide enablement for a method for treating and/or preventing cerebral ischemia comprising the step of administering to a subject in need thereof a medicament comprising as an active ingredient a hydrogenation production of *Boswellia serrata* obtained through the catalytic hydrogenation of ethanol extracts of frankincense (*Boswellia serrata*). The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims. Newly reapplied as necessitated by amendment and in view of Applicant's argument with regards to Applicant's elected specie "apoplexy".

Enablement is considered in view of the *Wands* factors (MPEP 2164.01(A)). These include: nature of the invention, breadth of the claims, guidance of the

specification, the existence of working examples, state of the art predictability of the art and the amount of experimentation necessary. All of the Wands factors have been considered with regard to the instant claims, with the most relevant factors discussed below.

Nature of the Invention: Claim 1 is drawn to a method of treating and/or preventing cerebral ischemia comprising the step of administering to a subject in need thereof a medicament comprising as an active ingredient a hydrogenation product of *Boswellia serrata* obtained through the catalytic hydrogenation of ethanol extracts of frankincense (*Boswellia serrata*). Claim 2 further claims that the cerebral ischemia of claim 1 occurs as a result of apoplexy.

The nature of the invention is complex in that claim 1 is drawn to a method of treating and/or preventing cerebral ischemia comprising the step of administering to a subject in need thereof a medicament comprising as an active ingredients a hydrogenation product of *Boswellia serrata* obtained through the catalytic hydrogenation of ethanol extracts of frankincense (*Boswellia serrata*). However, the way the claim is presently written, cerebral ischemia could result from any source and that regardless of the source, it can be treated or prevented. It should be noted that cerebral ischemia is an ischemic condition where the brain or parts of the brain do not receive enough blood flow to maintain normal neurological function and that cerebral ischemia can be the result of various diseases or the result of arterial obstruction, such as strangulation.

Breadth of the Claims: The claims are broad in that cerebral ischemia is treated and/or prevented in a subject comprising the step of administering to a subject in need

thereof a medicament comprising as an active ingredient a hydrogenation product of *Boswellia serrata* obtained through the catalytic hydrogenation of ethanol extracts of frankincense (*Boswellia serrata*). The complex nature of the subject matter of this invention is greatly exacerbated by the breadth of the claims.

Guidance of the Specification and Existence of Working Examples: The specification discloses a method of observing the effect of a frankincense extract containing boswellic acid on the infarct volume after experimentally induced transient focal cerebral ischemia (apoplexy), wherein Applicant discloses a method of experimental induction of a focal ischemia by intracerebral microinjection of endothelin 1 in the vicinity of the middle cerebral artery (eMCAO) and using Sprague Dawley rats, wherein the rats are intraperioneally injected with frankincense extract (See pages 16-19 of the originally filed specification). Please note that it appears that Applicant is disclosing a frankincense extract containing boswellic acid as the extract used in these trials. However, it should be noted that no other information is provided disclosing what the extract actually is or how it is obtained in the working examples, therefore, it is unclear for what Applicant is actually enabled.

Please note that while it is possible that damage from cerebral ischemia may be decreased, prevention of cerebral ischemia would require that a person is not exposed to any factors that could cause cerebral ischemia, such as strangulation. Therefore, Applicant is not enabled for prevention and/or treatment of cerebral ischemia.

Predictability and State of the Art: The state of the art at the time the invention was made was unpredictable and underdeveloped. For example, Singer et al. (U*,

'Associated systemic factors in cerebrovascular ischemia', South Med J. Vol. 69, No. 6 (June 1976) pp. 709-714) teaches that systematic disorders, such as cardiac disorders, are commonly recognized as predisposing and sometimes actual precipitating events in cerebral ischemia. Singer further teaches that a one-year comprehensive investigation of all patients with ischemic brain disease revealed that brain ischemia is more commonly precipitated by system illness than usually supposed, particularly transient ischemic attacks of the vertebrobasilar circulation and completed infarcts in the carotid distribution and that cardiac disorders outnumber all other precipitating events.

Braune et al. (V*, 'Cerebral infarct in the circulatory area of the arterial cerebrial media following chiropractic therapy of the cervical spine', Dtsch Med Wochenschr, Vol. 116, No. 27 (July 1991) pp. 1047-1050) teaches that chiropractic manipulation of the neck can occasionally cause severe neurological complications.

Based upon the fact that the actual underlying cause of cerebral ischemia is unknown, it is doubtful that Applicant's claimed invention can prevent cerebral ischemia, and that Applicant's invention can treat all types of cerebral ischemia, wherein cerebral ischemia or treat cerebral ischemia that occurs as a result of apoplexy.

Chen et al. (W*, "Combination therapy for ischemic stroke: potential of neuroprotectants plus thrombolytics". Am. J. Cardiovasc. Drugs, Vol. 2, No. 5 (2002) 303-313, Abstract only) teaches that cerebral ischemia triggers a number of pathophysiological and biochemical changes in the brain that present potential targets for therapeutic intervention. Although several neuroprotective agents which block cell death pathways have been proposed to have therapeutic potential in patients with

stroke (apoplexy) results from clinical trials have been disappointing. Finally, PCMR Research: Animal Experimentation Issues (X) teaches that stroke is the third leading cause of death in the U.S., but strokes and the conditions that lead to them are rare in rats and other animals. PCMR Research: Animal Experimentation Issues further teaches that animal "models" of stroke have been developed, but their usefulness has been severely criticized by the scientific community and that according to researchers at the University of Iowa and the Mayo Clinic in Rochester, Minnesota, although animal models of cerebral ischemia have been used extensively to test new therapies in human stroke, their record for identifying clinically effective drugs has been disappointing. PCMR Research: Animal Experimentation Issues further teaches of 25 compounds which were helpful in laboratory animal models of stroke, none worked on people and that an over-reliance upon such models may impede rather than advance scientific progress in the treatment of this disease. Therefore, irrespective of Applicant's working examples involving rats, it has not been established that rats are an adequate model for stroke in humans and there is no evidence that Applicant's claimed invention will have the desired effect in humans.

Thus, while the claim-designated method may be useful for providing such an effect, Applicant does not disclose a method of treating and/or preventing cerebral ischemia comprising the step of administering to a subject in need thereof a medicament comprising as an active ingredient a hydrogenation product of *Boswellia serrata* obtained through the catalytic hydrogenation of ethanol extracts of frankincense (*Boswellia serrata*).

Amount of Experimentation Necessary: The quantity of experimentation necessary to carry out the claimed invention is high, as the skilled artisan could not rely on the prior art or instant specification to teach how to make and use a medicament comprising hydrogenation products of frankincense extracts for treating and/or preventing cerebral ischemia or treating and/or preventing cerebral ischemia, wherein the cerebral ischemia occurs as a result of cardiac infarction in humans. In order to carry out the claimed invention, one of ordinary skill in the art would have to identify a medicament comprising hydrogenation products of frankincense extracts that can be administered in a therapeutically effective dose with an acceptable level of side-effects. Please note that the way the claims are currently written, that Applicant does not state that a therapeutically effective amount of a hydrogenation product of *Boswellia serrata* obtained through catalytic hydrogenation of ethanol extracts of frankincense (*Boswellia serrata*).

Finally, Applicant is not enabled for the ingredients of claims 12-14, since these compounds are not known in the art and Applicant has not provided any spectroscopic or experimental data showing that these compounds have Applicant's claimed effect or the effect known art at the time the invention was made.

In view of the breadth of the claims and the lack of guidance provided by the specification as well as the unpredictability of the art, the skilled artisan would have required an undue amount of experimentation to make and/or use the claimed invention. Therefore, claims 1-19 are not considered to be fully enabled by the instant specification.

This rejection is maintained for reasons of record set forth in the paper mailed on 07/27/2007 and repeated below, slightly altered to take into consideration Applicant's amendment filed on 12/21/2007.

Applicant's arguments have been thoroughly considered, but the rejection remains the same for the reasons set forth in the previous Office action and for the reasons set forth below.

In response to Applicant's argument that the Examiner's 112 1st paragraph rejection was written with regards to cardiac infarction and that Applicant had elected apoplexy, the argument is now rendered moot in view of the newly applied rejection above.

In response to Applicant's arguments regarding that Applicant provided working examples to confirm the utility of frankincense extracts in connection with the treatment of apoplexy, please note that Applicant has not provided any examples of what frankincense extract was used. Applicants simply define "frankincense extract" as a "frankincense extract containing boswellic acid". Secondly, in response to Applicant's argument that the Examiner must establish that enablement of how to make or use Applicant's invention has not been met, please note that the Examiner has provided evidence that there is no connection between rat models and humans with regards to treatment of strokes (See above) and, therefore, the burden has not been met by Applicant.

Please note the following art rejections are made based upon what was known in

the art at the time the invention was made. If not all claims are rejected under art, this does not mean that these claims are allowable, since all of the claims examined are rejected under 112 1st paragraph as lacking full enablement, as discussed above.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1, 3, 4, 7-9 and 16-19 are rejected under 35 U.S.C. 102(b) as being anticipated by Etzel (A*, US 5,720,975).

Etzel teaches a method of treating Alzheimer's disease comprising administering to a patient in need of such a treatment, an effective dosage of the medicament comprising at least one of the following: incense (olibanum), incense extract, biologically active substances contained in incense and boswellic acid (See abstract and claim 1). Etzel further teaches that the medicament can be administered orally, intraperitoneally, buccally, rectally, intramuscularly or topically and that the form of the medicament is a tablet, capsule, injectable solution, solution, salve, emulsion or creme (See claims 7 and 8). Etzel further teaches that *Boswellia serrata*, which reads on a boswellic-acid containing vegetable preparation and a frankinsense of boswellic acid-containing vegetable extract, is the preferred incense plant that contains boswellic acid and that the extracts are obtained by extraction with (4.2-5.9:1) chloroform: methanol (See

column 2, lines 34-46), which reads on the limitations of claims 3, 4, 7-9, 11 and 16-19.

Therefore, the reference anticipates the claimed subject matter.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1, 3-11 and 15-19 are rejected under 35 U.S.C. 103(a) as being unpatentable over Etzel (A*, US 5,720,975), in view of Badria et al. (U1).

The teachings of Etzel are set forth above and applied before. Etzel further teaches that incense resins may be used as a source of extracts, that the incense resin can be obtained from a *Boswellia* plant, wherein the *Boswellia* plant can be *Boswellia serrata* and that *Boswellia carterii*- misspelled by Etzel as *Boswellia carteri*- is also an

example of an incense plant useful in Etzel's invention). Please note that *Boswellia carterii* resin intrinsically contains 3-oxo-tirucallic acid, 3-hydroxy-tirucallic acid, β-boswellic acid and 11-keto-boswellic acid (See Badria et al.).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to modify the source of boswellic acid taught by Etzel because at the time the invention was made, it was known that Alzheimer's disease could be treated by administering to a patient in need of such a treatment, an effective dosage of a medicament comprising at least one of the following: incense (olibanum), incense extract, biologically active substances contained in incense and boswellic acid, as clearly taught by Etzel, as was that incense resins may be used as a source of extracts and that *Boswellia carterii* is also a useful source of incense (olibanum), incense extract, biologically active substances contained in incense and boswellic acid, as clearly taught by Etzel.

Finally, one of ordinary skill in the art would have been motivated and one would have had a reasonable expectation of success to use incense (olibanum), incense extract, biologically active substances contained in incense and boswellic acid obtained from *Boswellia carterii* or a resin of a *Boswellia* plant, wherein the *Boswellia* plant can be *Boswellia serrata* in a medicament for treating Alzheimer's disease, as clearly taught by Etzel.

Based upon the beneficial teachings of the cited references, the skill of one of ordinary skill in the art, and absent evidence to the contrary, there would have been a reasonable expectation of success to result in the claimed invention.

Accordingly, the claimed invention was *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, especially in the absence of evidence to the contrary.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Amy L. Clark whose telephone number is (571)272-1310. The examiner can normally be reached on Monday to Friday between 8:30am - 5pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Terry McKelvey can be reached on (571) 272-0775. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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July 29, 2008
/Michele Flood/
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